REMARKS

As a preliminary matter, the Attorney Docket No. of the present application has been changed to "UPN-4023."

The application as filed on October 5, 2000 contained amino acid sequences, which are now contained within the Sequence Listing. New pages 1-11, enclosed herewith, contain the Sequence Listing formatted under the new rules for submitting Sequence Listings, support for which can be found throughout the application as originally filed. The specification has been amended herein to insert the SEQ ID Numbers into the text to comply with rules set forth in 37 CFR §§1.821-1.825. No new matter has been added. The contents of the paper copy of the Sequence Listing and computer readable copy of the Sequence Listing, submitted in accordance with 37 CFR §1.821(c) and (e), are the same. In addition, please find enclosed herewith a Statement to Support Filing and Submission of DNA/Amino Acid Sequences in Accordance with 37 CFR §§1.821 through 1.825, and a computer readable form (CRF).

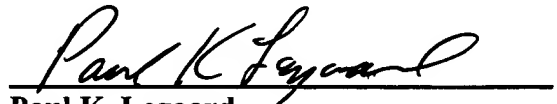
The Examiner has mistakenly restricted claims 1-27 into the following four groups: Group I (claims 1-11) drawn to conjugated compositions comprising Vpr linked to nucleic acids and methods of using the conjugated compound to deliver nucleic acids to a cell; Group II (claims 12-16 and 25-27) drawn to Vpr proteins as therapeutic compounds; Group III (claims 13, 14, and 17-20) drawn to Vpr conjugated to nucleic acids as therapeutic compounds; and Group IV (claims 21-24) drawn to methods of identifying compounds that inhibit Vpr binding to p6 protein. Applicants elect Group I, containing claims 1-11 **with traverse**.

The Office Action mistakenly asserts that Groups I-IV do not relate to a single general inventive concept because they lack the same or a corresponding special technical feature. § 803 of the M.P.E.P., however, mandates two criteria for a proper requirement for restriction: 1) the inventions must be independent or distinct; and 2) there must be a serious burden on the examiner. For purposes of initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in M.P.E.P. §808.02. Significantly, the Examiner has not met the *prima facie* burden. Indeed, the Examiner has not shown separate classification, separate

status in the art, or a requirement for a different field of search. Accordingly, *all pending claims* should be examined in the present application without restriction.

Applicants submit that the present response is complete and complies with the requirements of 35 U.S.C. § 121. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Application:

New pages 1-11 containing the Sequence Listing have been added.

In the Specification:

Paragraph beginning at page 5, line 17 of the specification has been amended as follows:

--Figures 1A-1D show construction and expression of mutant Vpr molecules. Figure 1A shows an amino acid sequence comparison of Vpr of HIV-1 (SEQ ID NO: 1) and 2/SIV (SEQ ID NO:2) and Vpx of HIV-2/SIV (SEQ ID NO:3). Numbers denote positions of amino acid residues for each protein sequence provided. Figure 1B shows expression plasmids for the synthesis of mutant Vpr molecules were generated by overlap Polymerase Chain Reaction (PCR) at the indicated codons. PCR-amplified mutant vpr gene fragments were digested with *HindIII and XhoI* and ligated to pCDNA3 vector to produce Vpr mutant expression plasmids. VPR wt is SEQ ID NO:4; E21,24P is SEQ ID NO:5; αL-A is SEQ ID NO:6; A30S is SEQ ID NO:7; A30L is SEQ ID NO:8; A59P is SEQ ID NO:9; L64S is SEQ ID NO:10; L67S is SEQ ID NO:11; L68S is SEQ ID NO:12; H71C is SEQ ID NO:13; H71Y is SEQ ID NO:14; G75A is SEQ ID NO:15; C76S is SEQ ID NO:16; and HXB2 is SEQ ID NO:17. Figure 1C shows recombinant vaccinia virus (vTF7-3) infected HeLa cells were transfected with wild type and mutant vpr expression plasmids. Transfected cells were labeled with S^{35} protein labeling mix for 2 hours and the cell-associated Vpr proteins were immunoprecipitated with anti-Vpr antiserum as described in Materials and Methods. Immunoprecipitates were analyzed by SDS-12% PAGE. The designation of the Vpr plasmids is indicated at the top. Figure 1D shows the secondary structure of Vpr (SEQ ID NO:18) was calculated using the program *nnpredict* (Kneller, D.G. et al., *J. Mol. Biol.*, **1990**, *214:* 171-182.). *nnpredict* is a program that predicts the secondary structure type for each residue in an amino acid sequence based on the prediction of a two-layer, feed-forward neural network. H is helical, E is extended and dash (-) is undefined. αL-A, L64S, and H71C display the same secondary profile as the Vpr wild-type, suggesting the importance of the Leu residues on the hydrophobic face and His in the C-

terminus. Introduction of proline-residue in E21, E24 and A59 disrupt the respective helical domains.--